REMARKS/ARGUMENTS

The Status of the Claims.

Claims 1, 3-5, 14-15, 34-40, 43-44, and 53-69 are pending with entry of this amendment. Claims 68 and 69 have been amended to further clarify the claimed invention. These amendments introduce no new matter and support for the amendment is replete throughout the specification and claims as originally filed. These amendments are made without prejudice and are not to be construed as abandonment of the previously claimed subject matter, or agreement with any objection or rejection of record. Applicants respectfully request entry of these amendments prior to examination of the above-identified application.

The Specification.

Applicants have amended the specification to incorporate the ATCC deposit information. Accompanying this Amendment is the "Statement Regarding Biological Deposit" from inventor Dr. James D. Marks, corroborating that ATCC deposit PTA-7843 encodes the F5 internalizing antibody described and claimed in the subject invention.

Per CFR §1.804(a), the ATCC deposit was made during pendency of the application for patent. Applicants submit that these amendments introduce no new matter, are made without prejudice and are not to be construed as abandonment of the previously claimed subject matter or agreement with any objection or rejection of record. Accordingly, entry of the Amendment is respectfully requested.

Examiner Interview.

Applicants respectfully thank Examiner Ungar and Supervisory Examiner Siew for the helpful discussion and input in the telephonic Examiner Interview held October 23, 2006. Agreement was reached with Examiners Ungar and Siew that correction of the sequence listing would be allowable. Examiners Ungar and Siew also discussed the issue with Biotech Practice Specialist Christopher Low (who, incidentally, was the Examiner of record in *Ex parte Maizel*); Biotech Practice Specialist Low also indicated that revision to the sequence listing would be allowed given the appropriate chain of evidence.

Sequence Listing Submission

Per the Examiner's request, accompanying this Amendment is a Substitute Sequence Listing, amending the sequence listing to correct a typographical error in the nucleotide sequence of F5 (SEQ ID NO:3) and the corresponding polypeptide sequence (SEQ ID NO:1). The Sequence Listing has been amended as follows:

In SEQ ID NO:1, Phe has been replaced with Ser at amino acid position 226.

In SEQ ID NO:3, T has been replaced with C at nucleotide position 677.

The undersigned hereby states that the Sequence Listing submitted concurrently herewith does not include matter which goes beyond the content of the application as filed. The above amendment merely corrects a typographical error in the Sequence Listing, and therefore introduces no new matter.

Comparison to Ex parte Maizel

Applicants note, per the discussion held with Examiner Ungar and Supervisory Examiner Siew on October 23, 2006, that the facts in the present application do not parallel those in *Ex parte Maizel*. As such, Applicants respectfully submit that amendment of the sequence listing does not represent incorporation of new matter into the specification, but rather is only a correction of structural formula (in this case, the identity of a single nucleiotide in SEQ ID NO:3 and the corresponding amino acid in SEQ ID NO:1)

In *Ex parte Maizel*, Applicants had attempt to amend the sequences provided in the specification to correct three separate errors that resulted in a frameshift reading error of a predicted polypeptide sequence (i.e., the identity of the amino acids in the predicted N-terminal portion of the polypeptide were incorrectly determined from the nucleotide sequence). The Examiner rejected the sequence amendment as new matter; the Court upheld this finding, in light of the badly mis-described sequences and the position that the chain of evidence had been broken (the source of sample that was re-sequenced was not shown to be the same as that deposited with the ATCC). However, despite the rejection of the sequence amendments as new matter, the Court also noted that:

> Mechanism within Patent and Trademark Office for correcting DNA sequencing errors in specification is highly desirable, since such errors may well arise, but no general rule can be

> established because question of whether or not change in chemical structure of DNA sequences set forth in specification is permitted depends upon facts of each case and significance of modification to both subject matter claimed and subject matter described in specification.

Applicants respectfully submit that, in light of the minor extent of the seqeuncing error in the subject application and the clear chain of evidence provided herein, the facts in the present application do not parallel those in *Ex parte Maizel*.

When the F5 plasmid (ATCC deposit PTA-7843) was sequenced by collaborators at the National Institutes of Health (in preparation for for pre-clinical analysis), and subsequently re-sequenced by the inventors, an error was found in the F5 sequence listing as originally filed: the amino acid at position 226 in SEQ ID NO:1 was incorrectly identified as a phenylalanine instead of a serine. The typographical error was inadvertently introduced during use of an automated sequence reader to read the original sequencing gel; manual inspection *of the original sequencing gel data* confirmed that nucleotide 677 in SEQ ID NO:3 had been incorrectly read as a thymine (T) instead of a cytosine (C), leading to incorrect identification of amino acid 226 as phenylalanine (TTC) instead of serine (TCC) in SEQ ID NO:1. The error was a substitution-type error, and not a frameshift error; the identity of only one amino acid in the polypeptide was affected by the misread gel.

Amendment of the sequence listing to correct the typographical error should not be considered new matter, since the facts in the present application do not parallel those in *Ex parte Maizel*. First, as noted above, only a single amino acid identity was affected by the error in the automated gel reader; not frameshift errors which alter large sections of polypeptide sequence as seen in Maizel. Second, unlike *Maizel*, there is a clear chain of evidence in the present application. The original sequencing gel data chromatogram had the correct information (and thus, Applicants were in possession of the information at the time of filing), and the ATCC deposit was made using the exact same material as described in the specification. Furthermore, the sequencing information was confirmed using this same plasmid, which had been archived by the researchers at NIH (and subsequently returned to Applicants to facilitate submission to the ATCC). Thus, the biological material deposited with

the ATCC and accorded patent deposit designation PTA-7843 is the same plasmid as described in the subject application.

As noted in *Ex parte Marsili* (which was also cited in *Ex parte Maizel*):

> Refusing to correct structural formula of Applicant's claimed compounds that have been found patentable by Examiner would lead to absurdity of issuing patent that teaches public, in its specification, wrong scientific formula for new products.

Applicants respectfully request that the substitute sequence listing, correcting the nucleotide error in SEQ ID NO: 3, and the corresponding amino acid in SEQ ID NO:1, be entered, rather than issuance of a patent that teaches the public incorrect sequence information for the F5 antibody. A computer readable format (txt file) of the Substitute Sequence Listing is submitted herewith.

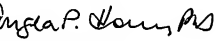
CONCLUSION

Applicants respectfully request that the amendments the claims and specification be entered, and that the inadvertent typographical error in the sequence listing be corrected. Applicants believe all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the claims are deemed not to be in condition for allowance after consideration of this Response, a telephone interview with the Examiner is hereby requested. Please telephone the undersigned at (510) 337-7871 to schedule an interview.

QUINE INTELLECTUAL PROPERTY LAW GROUP
P.O. BOX 458, Alameda, CA 94501
Tel: 510 337-7871
Fax: 510 337-7877
PTO Customer No.: **22798**
Deposit Account No.: **50-0893**

Respectfully submitted,



Angela P. Horne, Ph.D.
Reg. No: 41,079

Attachments:

1) A transmittal sheet;
2) Copy of ATCC plasmid deposit receipt;
3) Inventor Statement regarding Biological Deposit;
4) Inventor Statement regarding Sequence Error;
5) Supplemental Sequence Listing;

407J-8950-30 US

ATCC

10801 University Blvd • Manassas, VA 20110-2209 • Telephone: 703-365-2700 • FAX: 703-365-2745

BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE

INTERNATIONAL FORM

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT ISSUED PURSUANT TO RULE 7.3 AND VIABILITY STATEMENT ISSUED PURSUANT TO RULE 10.2

To: (Name and Address of Depositor or Attorney)

Linda S. Stevenson
1111 Franklin St., 12th Floor
Oakland, CA 94607-5200

Deposited on Behalf of: The Regents of the University of California

Identification Reference by Depositor:	**Patent Deposit Designation**
Anti-HER 2 single chain Fv antibody F5 in plasmid pSYN1: E.coli DH5alpha	PTA-7843

The deposit was accompanied by: X a scientific description __ a proposed taxonomic description indicated above.

The deposit was received August 24, 2006 by this International Depository Authority and has been accepted.

AT YOUR REQUEST: X We will inform you of requests for the strain for 30 years.

The strain will be made available if a patent office signatory to the Budapest Treaty certifies one's right to receive, or if a U.S. Patent is issued citing the strain, and ATCC is instructed by the United States Patent & Trademark Office or the depositor to release said strain.

If the culture should die or be destroyed during the effective term of the deposit, it shall be your responsibility to replace it with living culture of the same.

The strain will be maintained for a period of at least 30 years from date of deposit, or five years after the most recent request for a sample, whichever is longer. The United States and many other countries are signatory to the Budapest Treaty.

The viability of the culture cited above was tested September 8, 2006 . On that date, the culture was viable.

International Depository Authority: American Type Culture Collection, Manassas, VA 20110-2209 USA.

Signature of person having authority to represent ATCC:

Dee Bishop, ATCC Patent Depository **Date: September 12, 2006**

cc: Angela P. Horne (Ref: Docket or Case # : 407J-895030US)

CERTIFICATE OF MAILING
I hereby certify that this correspondence is being deposited with the United States Postal Service first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on _____.

QUINE INTELLECTUAL PROPERTY LAW GROUP, P.C.

By:_____

Appl. No.	:	09/250,056	Confirmation No. 1647
Applicant	:	James D. Marks, et al.	
Filed	:	February 12, 1999	
TC/A.U.	:	1642	
Examiner	:	Susan Ungar	

Docket No. : 407J-895030US
Customer No. : 22798
Client Ref No.: 98-232-4

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

STATEMENT REGARDING BIOLOGICAL DEPOSIT

Sir:

Pursuant to 37 CFR §1.804, the biological material which has been deposited with the American Type Culture Collection (ATCC) and accorded plasmid deposit designation **PTA-7843** encodes internalizing antibody F5, a biological material as specifically identified in the application as filed.

As an inventor and as the person who made the deposit, I am able to corroborate that the biological material deposited the ATCC is the same plasmid as used to generate the F5 polypeptide used in the experiments described in the specification. With respect to the chain of custody, the plasmid encoding F5 and used in the experiments as provided in the specification was also sent to the National Institutes of Health for experimental use and analysis. The F5 plasmid, which had been catalogued and stored by the investigators at the NIH, was subsequently returned to Applicants to facilitate submission to the ATCC.

Signature: _____ 12/4/06

Name: James D. Marks, MD, Ph.D.
Title: Professor in Residence, Dept. of Anesthesia and Pharmaceutical Chemistry
University of California San Francisco

CERTIFICATE OF MAILING

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QUINE INTELLECTUAL PROPERTY LAW GROUP, P.C.

By:_____

Appl. No. : 09/250,056 Confirmation No. 1647
Applicant : James D. Marks, et al.
Filed : February 12, 1999
TC/A.U. : 1642
Examiner : Susan Ungar

Docket No. : 407J-895030US
Customer No. : 22798
Client Ref No.: 98-232-4

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

INVENTOR STATEMENT REGARDING SEQUENCE ERROR

Sir:

Upon notification that an error had been found in the F5 sequence, our lab reviewed the original sequencing gel data (chromatogram). Manual inspection of the original gel chromatogram confirmed that nucleotide 677 in SEQ ID NO:3 had been incorrectly read by the automated sequence gel reader as a thymine (T) instead of a cytosine (C), leading to incorrect identification of amino acid 226 as phenylalanine (TTC) instead of serine (TCC) in SEQ ID NO:1. The error was a substitution-type error, and not a frameshift error; the identity of only one amino acid in the polypeptide was affected by the misread gel.

We have also re-sequenced the F5 sequence encoded by ATCC deposit PTA-7843, and confirmed that the nucleotide at position 677 is a cytosine (and not a thymine as originally indicated using the automated gel reader). Furthermore, as an inventor, I am able to corroborate that the F5 polypeptide used in the experiments described in the specification had a serine at position 226, and not a phenylalanine.

Signature: _____

Name: James D. Marks, MD, Ph.D.
Title: Professor in Residence, Dept. of Anesthesia and Pharmaceutical Chemistry
University of California San Francisco